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| capsule adj5 amine | 120 |

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| <i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR</i> | | |
| <u>L12</u> capsule adj5 amine | 120 | <u>L12</u> |
| <u>L11</u> cox\$2 same capsule same \$amine | 14 | <u>L11</u> |
| <u>L10</u> cox\$2 same capsule same amine | 14 | <u>L10</u> |
| <u>L9</u> L7 and sulfite | 40 | <u>L9</u> |
| <u>L8</u> L7 and (amino adj1 acid) | 136 | <u>L8</u> |
| <u>L7</u> cox\$2 same capsule | 365 | <u>L7</u> |
| <u>L6</u> cox\$2 same (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) same capsule | 12 | <u>L6</u> |
| <u>L5</u> cox\$ same (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) same capsule same (stabiliz\$ or cross\$) | 3 | <u>L5</u> |
| <u>L4</u> L3 and cyclooxygenase\$ | 19 | <u>L4</u> |
| (ethanolamine or \$diamine or amino or benethamine or benzathine or | | |

| | | | |
|-----------|---|-----|-----------|
| <u>L3</u> | piperazine or hydrabamine or imidazole) same capsule same (stabiliz\$ or cross\$) | 895 | <u>L3</u> |
| <u>L2</u> | (celecoxib or deracoxib or valdecoxib or rofecoxib or etoricoxib) same (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) and capsule | 261 | <u>L2</u> |
| <u>L1</u> | (celecoxib or deracoxib or valdecoxib or rofecoxib or etoricoxib) same (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) same capsule | 12 | <u>L1</u> |

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Search Results - Record(s) 1 through 12 of 12 returned.

☐ 1. Document ID: US 20060178435 A1

L1: Entry 1 of 12

File: PGPB

Aug 10, 2006

PGPUB-DOCUMENT-NUMBER: 20060178435

PGPUB-FILING-TYPE:

DOCUMENT-IDENTIFIER: US 20060178435 A1

TITLE: Apogossypolone and the uses thereof

PUBLICATION-DATE: August 10, 2006

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY |
|----------------------------|-----------|-------|---------|
| Wang; Shaomeng | Saline | MI | US |
| Chen; Jianyong | Ann Arbor | MI | US |
| Nikolovska-Coleska; Zaneta | Ann Arbor | MI | US |
| Yang; Dajun | Rockville | MD | US |

US-CL-CURRENT: [514/548](#); [514/682](#), [552/298](#)

| | | | | | | | | | | | | |
|----------------------|-----------------------|--------------------------|-----------------------|------------------------|--------------------------------|----------------------|---------------------------|---------------------------|-----------------------------|------------------------|---------------------|--------------------------|
| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | RMC | Drawings |
|----------------------|-----------------------|--------------------------|-----------------------|------------------------|--------------------------------|----------------------|---------------------------|---------------------------|-----------------------------|------------------------|---------------------|--------------------------|

☐ 2. Document ID: US 20060166920 A1

L1: Entry 2 of 12

File: PGPB

Jul 27, 2006

PGPUB-DOCUMENT-NUMBER: 20060166920

PGPUB-FILING-TYPE:

DOCUMENT-IDENTIFIER: US 20060166920 A1

TITLE: Oligonucleotide based therapeutics

PUBLICATION-DATE: July 27, 2006

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY |
|-----------|-----------|-------|---------|
| Xu; Liang | Ann Arbor | MI | US |

| | | | |
|------------------|-----------|----|----|
| Lippman; Marc E. | Ann Arbor | MI | US |
| Liu; Meilan | Ann Arbor | MI | US |

US-CL-CURRENT: 514/44

| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | PubC | Draw D. |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|---------|
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|---------|

☐ 3. Document ID: US 20060127376 A1

L1: Entry 3 of 12

File: PGPB

Jun 15, 2006

PGPUB-DOCUMENT-NUMBER: 20060127376

PGPUB-FILING-TYPE:

DOCUMENT-IDENTIFIER: US 20060127376 A1

TITLE: Methods and compositions for modulating apoptotic pathways

PUBLICATION-DATE: June 15, 2006

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY |
|-----------|----------|-------|---------|
| Moll; Ute | Setauket | NY | US |

US-CL-CURRENT: 424/93.21; 514/44

| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | PubC | Draw D. |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|---------|
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|---------|

☐ 4. Document ID: US 20060084647 A1

L1: Entry 4 of 12

File: PGPB

Apr 20, 2006

PGPUB-DOCUMENT-NUMBER: 20060084647

PGPUB-FILING-TYPE:

DOCUMENT-IDENTIFIER: US 20060084647 A1

TITLE: Small molecule inhibitors of anti-apoptotic BCL-2 family members and the uses thereof

PUBLICATION-DATE: April 20, 2006

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY |
|----------------------------|-----------|-------|---------|
| Wang; Shaomeng | Saline | MI | US |
| Wang; Guoping | Ann Arbor | MI | US |
| Tang; Guozhi | Ann Arbor | MI | US |
| Wang; Renxiao | Ann Arbor | MI | US |
| Nikolovska-Coleska; Zaneta | Ann Arbor | MI | US |
| Yang; Dajun | Rockville | MD | US |
| Xu; Liang | Ann Arbor | MI | US |

US-CL-CURRENT: [514/232.5](#); [514/252.14](#), [514/308](#), [514/310](#), [514/319](#), [514/618](#), [514/621](#),
[514/688](#), [544/128](#), [544/295](#), [546/140](#), [546/205](#), [564/162](#), [564/170](#), [568/325](#)

| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | RWDC | Draw D- |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|---------|
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☐ 5. Document ID: US 20060078903 A1

L1: Entry 5 of 12

File: PGPB

Apr 13, 2006

PGPUB-DOCUMENT-NUMBER: 20060078903

PGPUB-FILING-TYPE:

DOCUMENT-IDENTIFIER: US 20060078903 A1

TITLE: Methods and compositions for the diagnosis and treatment of cyclin A-1 associated conditions

PUBLICATION-DATE: April 13, 2006

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY |
|---------------------|-----------|-------|---------|
| Ford; Heide L. | Denver | CO | US |
| Coletta; Ricardo D. | Sao Paulo | MA | BR |
| Pardee; Arthur R. | Cambridge | MA | US |
| Lamb; Justin | Cambridge | | US |

US-CL-CURRENT: [435/6](#); [435/7.23](#)

| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | RWDC | Draw D- |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|---------|
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|---------|

☐ 6. Document ID: US 20050288239 A1

L1: Entry 6 of 12

File: PGPB

Dec 29, 2005

PGPUB-DOCUMENT-NUMBER: 20050288239

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20050288239 A1

TITLE: Anticancer glycoside compounds

PUBLICATION-DATE: December 29, 2005

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY |
|-------------------|---------|-------|---------|
| Adrian, Thomas E. | Chicago | IL | US |
| Collin, Peter D. | Sunset | ME | US |

US-CL-CURRENT: [514/33](#); [424/756](#)

| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | RWDC | Draw D- |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|---------|
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☐ 7. Document ID: US 20050261232 A1

L1: Entry 7 of 12

File: PGPB

Nov 24, 2005

PGPUB-DOCUMENT-NUMBER: 20050261232

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20050261232 A1

TITLE: Non-natural ribonuclease conjugates as cytotoxic agents

PUBLICATION-DATE: November 24, 2005

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY |
|------------------|-----------|-------|---------|
| Strong, Laura E. | Stoughton | WI | US |
| Leland, Peter A. | Fitchburg | WI | US |
| Burke, Thomas | Madison | WI | US |

US-CL-CURRENT: 514/44; 424/155.1

| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | EMC | Draw D |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|-----|--------|
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☐ 8. Document ID: US 20050234135 A1

L1: Entry 8 of 12

File: PGPB

Oct 20, 2005

PGPUB-DOCUMENT-NUMBER: 20050234135

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20050234135 A1

TITLE: Gossypol co-crystals and the use thereof

PUBLICATION-DATE: October 20, 2005

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY |
|-----------------|-----------|-------|---------|
| Wang, Shaomeng | Saline | MI | US |
| Chen, Jiangyong | Ann Arbor | MI | US |

US-CL-CURRENT: 514/700

| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | EMC | Draw D |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|-----|--------|
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|-----|--------|

☐ 9. Document ID: US 20050232927 A1

L1: Entry 9 of 12

File: PGPB

Oct 20, 2005

PGPUB-DOCUMENT-NUMBER: 20050232927

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20050232927 A1

TITLE: Compositions and methods for characterizing, regulating, diagnosing, and treating cancer

PUBLICATION-DATE: October 20, 2005

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY |
|--------------------|-----------|-------|---------|
| Clarke, Michael F. | Ann Arbor | MI | US |
| Al-Hajj, Muhammad | Cambridge | MA | US |

US-CL-CURRENT: 424/155.1; 435/7.23, 514/12

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|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|----------|
| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | RIMC | Drawings |
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☐ 10. Document ID: US 20050187276 A1

L1: Entry 10 of 12

File: PGPB

Aug 25, 2005

PGPUB-DOCUMENT-NUMBER: 20050187276

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20050187276 A1

TITLE: Compounds, compositions and methods

PUBLICATION-DATE: August 25, 2005

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY |
|-----------------|-------------|-------|---------|
| Park, Jong-Wan | Sung bok gu | CA | KR |
| Chun, Yang-Sook | Sung bok gu | CA | KR |
| Bair, Kenneth | Oakland | | US |
| Cho, Ho Sung | San Diego | | US |

US-CL-CURRENT: 514/396; 514/406

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|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|----------|
| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | RIMC | Drawings |
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☐ 11. Document ID: US 20040214902 A1

L1: Entry 11 of 12

File: PGPB

Oct 28, 2004

PGPUB-DOCUMENT-NUMBER: 20040214902

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040214902 A1

TITLE: Small molecule antagonists of BCL-2 family proteins

PUBLICATION-DATE: October 28, 2004

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY |
|----------------|-----------|-------|---------|
| Wang, Shaomeng | Saline | MI | US |
| Yang, Dajun | Rockville | MD | US |

US-CL-CURRENT: 514/700

| | | | | | | | | | | | | |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|---------|
| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | RmJC | Draw D. |
|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|---------|

☐ 12. Document ID: US 20040105883 A1

L1: Entry 12 of 12

File: PGPB

Jun 3, 2004

PGPUB-DOCUMENT-NUMBER: 20040105883

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040105883 A1

TITLE: Pharmaceutical dosage form capable of maintaining stable dissolution profile upon storage

PUBLICATION-DATE: June 3, 2004

INVENTOR-INFORMATION:

| NAME | CITY | STATE | COUNTRY |
|-------------------|-----------|-------|---------|
| Gao, Ping | Portage | MI | US |
| Bauer, Juliane M. | Portage | MI | US |
| He, Xiaorong | Kalamazoo | MI | US |

US-CL-CURRENT: 424/452; 424/456

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|------|-------|----------|-------|--------|----------------|------|-----------|-----------|-------------|--------|------|---------|
| Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | RmJC | Draw D. |
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| Terms | Documents |
|---|-----------|
| (celecoxib or deracoxib or valdecoxib or rofecoxib or etoricoxib) same (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) same capsule | 12 |

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L2: Entry 258 of 261

File: USPT

Jun 17, 2003

DOCUMENT-IDENTIFIER: US 6579895 B2

TITLE: Use of a celecoxib composition for fast pain relief

Brief Summary Text (6):

Celecoxib is well known as a highly effective selective COX-2 inhibitory drug and is widely prescribed for treatment of chronic inflammatory diseases such as rheumatoid arthritis and osteoarthritis. Celecoxib is available under the trademark Celebrex.RTM. of Pharmacia Corporation in capsule dosage forms containing 100 mg or 200 mg of the drug. Although these dosage forms can provide very effective relief of pain, they can, at least in some acute pain situations, exhibit a slower onset of pain relief than a standard NSAID such as ibuprofen.

Brief Summary Text (7):

A suspension of particulate celecoxib in a vehicle of apple juice is disclosed in Ecuador Patent Application No. 98-2761 ("EC 98-2761" which corresponds to WO 00/32189, Jun. 8, 2000). See in particular Example 13 therein, which describes preparation of such a suspension by dissolving celecoxib in ethanol containing 5% polysorbate 80 and adding the resulting mixture to apple juice prior to oral administration to 10 healthy male subjects. The dose administered was 300 mg celecoxib. An equal 300 mg dose was administered for comparison, in the form of three 100 mg capsules containing formulated celecoxib having a D.sub.90 particle size of about 37 .mu.m (i.e., 90% by weight of celecoxib particles in the formulation were smaller, in their longest dimension, than about 37 .mu.m). Pharmacokinetic parameters disclosed indicate that the suspension gave a higher C.sub.max, shorter T.sub.max and shorter T.sub.1/2 than the capsules as indicated in Table 1 below, where C.sub.max is the average maximum blood plasma concentration of celecoxib following administration, T.sub.max is the average length of time from administration until C.sub.max is reached, and T.sub.1/2 is the average terminal half-life of blood plasma concentration of celecoxib following T.sub.max.

Brief Summary Text (8):

Ibuprofen in a typical acute pain relief dose of 400 mg normally provides an adequate level of suppression of pain, for example post-surgical pain, by about 1 hour after administration. Celecoxib in capsule form normally takes longer, for example about 2 hours, to achieve a similar level of pain suppression. No suggestion is made in above-cited EC 98-2761 that the apparently modest reduction in T.sub.max exhibited by the disclosed suspension by comparison with the capsule formulation, when administered in a 300 mg dose, could be associated with a major improvement in onset of pain relief, or that the suspension formulation of celecoxib could be at least comparable with ibuprofen in onset of pain relief.

Brief Summary Text (9):

Above-cited EC 98-2761 merely discloses in general terms that compositions of the invention disclosed therein, i.e., including the disclosed capsule formulations as well as the suspension composition of Example 13 thereof, are effective "for pain management generally (particularly post-oral surgery pain, post-general surgery pain, post-orthopedic surgery pain, and acute flares of osteoarthritis)". Nevertheless, this reference contains no suggestion that the suspension composition might provide an effective pain relieving amount of celecoxib nor was it appreciated by this reference that an effective pain-relieving concentration of 250

nm/ml plasma or greater could be achieved in a rapidly bioavailable formulation. This is particularly in view of the extensive binding of celecoxib to plasma albumin which was known to occur following oral administration (Davies et al., Clin. Pharmacokinet. 38:225-242, 2000). Thus, one could not have predicted that a particular plasma concentration would produce analgesia.

Brief Summary Paragraph Table (1):

TABLE 1 Pharmacokinetics of celecoxib suspension and capsule formulations (from Ecuador Patent Application No. 98-2761) 300 mg celecoxib 300 mg celecoxib as suspension as capsules C.sub.max (ng/ml 1526.5 1076.5 plasma) T.sub.max (h) 1.42 1.94 T.sub.1/2 (h) 11.53 15.57

Drawing Description Text (2):

FIG. 1 shows blood plasma concentration profiles of celecoxib administered as a single oral dose of 200 mg, in the form of a capsule (Celebrex.RTM. 200 mg, Pharmacia Corporation) or in the form of a fine suspension in apple juice as described in Example 1.

Drawing Description Text (3):

FIG. 2 shows relief of post-surgical pain experienced over a 12-hour period following administration of a single oral dose of (1) 200 mg celecoxib in the form of a capsule (Celebrex.RTM. 200 mg, Pharmacia Corporation), (2) 400 mg ibuprofen in the form of a capsule, (3) 200 mg celecoxib in the form of a fine suspension in apple juice as described in Example 1, or (4) placebo.

Drawing Description Text (5):

FIG. 4 shows blood plasma concentration profiles of celecoxib administered as a single oral dose of 200 mg, in the form of a capsule (Celebrex.RTM. 200 mg, Pharmacia Corporation), in the form of a suspension in apple juice as described in Example 2, or in the form of Test Composition 1 of Example 2.

Detailed Description Text (12):

In yet another particularly preferred embodiment the formulation exhibits, in comparative pharmacokinetic testing versus a standard commercial formulation of celecoxib, such as Celebrex.RTM. 200 mg capsules of Pharmacia Corporation, a T.sub.max not greater than about 50%, even more preferably not greater than about 33%, and most preferably not greater than about 25%, of the T.sub.max exhibited by said standard commercial formulation.

Detailed Description Text (26):

Finely divided particulate or nanoparticulate celecoxib is not necessarily administered in suspension. It can be administered as a solid dosage form such as a capsule or tablet, provided disintegration of the solid dosage form to release celecoxib into the gastrointestinal fluid occurs rapidly enough to generate the presently desired pharmacokinetic profile. Similarly, a solution of celecoxib can be administered in a capsule, such as a hard or soft capsule having a wall comprising gelatin or hydroxypropylmethylcellulose (HPMC), provided the capsule wall dissolves or disintegrates rapidly enough in gastrointestinal fluid to enable the celecoxib thus released to be absorbed into the bloodstream and generate the presently desired pharmacokinetic profile.

Detailed Description Text (48):

Celecoxib compositions useful in methods of the present invention can be used in combination therapies with opioids and other analgesics, including narcotic analgesics, Mu receptor antagonists, Kappa receptor antagonists, non-narcotic (i.e., non-addictive) analgesics, monoamine uptake inhibitors, adenosine regulating agents, cannabinoid derivatives, Substance P antagonists, neurokinin-1 receptor antagonists and sodium channel blockers, among others. Preferred combination therapies comprise a composition useful in methods of the invention with one or more compounds selected from aceclofenac, acemetacin, e-acetamidocaproic acid,

Detailed Description Text (59):

http://jupiter:9000/bin/gate.exe?f=doc&state=8pn405.17.258&ESNAME=KWIC&p Messag... 9/11/06

Placebo.

Detailed Description Text (64):

The profile of blood plasma concentration of celecoxib in patients receiving the celecoxib dosage forms is shown for both dosage forms in FIG. 1. It will be noted that with the suspension, a blood plasma concentration greater than 300 ng/ml was attained just 15 minutes after administration, whereas with the commercial capsule it took over 2 hours to reach this concentration. Absorption of celecoxib from the suspension was therefore much faster than from the capsule formulation. Calculated T.sub.max for the suspension was 0.88 hours (i.e., about 53 minutes), compared to 3.86 hours for the capsule. C.sub.max for the suspension was 703 ng/ml, by comparison with 548 ng/ml for the capsule. Overall bioavailability, as measured by an integral function of blood plasma concentration over 24 hours, i.e., area under the curve, or AUC.sub.0-24 h, was similar for the two formulations.

Detailed Description Text (66):

Progression of pain relief during the first two hours after administration is more clearly seen in FIG. 3. It will be seen that the celecoxib 200 mg suspension (treatment 3) began to show improved pain relief over placebo (treatment 4) as early as 15 minutes after administration. The first clear sign that ibuprofen 400 mg capsule (treatment 2) was giving greater pain relief than placebo was seen 30 minutes after administration, and the first clear sign that celecoxib 200 mg capsule (treatment 1) was giving greater pain relief than placebo was seen 45 minutes after administration.

Detailed Description Text (67):

A mean pain relief score approaching 2 was first seen with celecoxib suspension (treatment 3) at 30 minutes, with ibuprofen capsule (treatment 2) at 1 hour and with celecoxib capsule (treatment 1) at 1.5-2 hours after administration. The pain relief score obtained with celecoxib suspension was statistically significantly superior to that obtained with ibuprofen capsule at all times up to and including 1 hour after administration.

Detailed Description Text (68):

Median time to onset of analgesia as recorded by the patients was 19 minutes for celecoxib suspension, 28 minutes for ibuprofen capsule, 40 minutes for celecoxib capsule, and >24 hours for placebo.

Detailed Description Text (72):

One gram of formulation SF-1 was individually placed into each of several hard gelatin capsules (Capsugel) to form Test Composition 1.

Detailed Description Text (74):

Bioavailability parameters resulting from administration of Test Composition 1, in comparison with the above-described comparative celecoxib suspension and with a commercial celecoxib (Celebrex.RTM. of Pharmacia) 200 mg capsule, to human subjects were evaluated in a 24-subject, randomized, four period, balanced, crossover study. Study duration was approximately 15 days and subjects were randomly given one of each of the four dosage forms on days 1, 5, 9 and 12; administration of each dose was preceded by an 8 hour fasting period and was accompanied by 180 ml of water. Plasma blood levels for each subject were measured at pre-dose and at 15, 30, 45 minutes and 1, 1.5, 2, 3, 4, 6, 8, 12 and 24 hours after dosage administration. C.sub.max and AUC were calculated from the data in accordance with standard procedure in the art. As shown in FIG. 4, ingestion of Test Composition 1 resulted in a C.sub.max more than 2.5 times greater than resulted from ingestion of the comparative celecoxib suspension or the commercial celecoxib capsule. Ingestion of Test Composition 1 also resulted in an AUC 43% greater than, and a T.sub.max substantially similar to, that resulting from ingestion of the comparative celecoxib suspension.

CLAIMS:

18. The method of claim 16 wherein the celecoxib formulation is encapsulated as a unit dosage form having a capsule wall.

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L4

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| | <i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR</i> | | |
| <u>L4</u> | L3 and cyclooxygenase\$ (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) same capsule same (stabiliz\$ or cross\$) | 19 | <u>L4</u> |
| <u>L3</u> | (celecoxib or deracoxib or valdecoxib or rofecoxib or etoricoxib) same (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) and capsule | 895 | <u>L3</u> |
| <u>L2</u> | (celecoxib or deracoxib or valdecoxib or rofecoxib or etoricoxib) same (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) same capsule | 261 | <u>L2</u> |
| <u>L1</u> | (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) same capsule | 12 | <u>L1</u> |

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Search Results - Record(s) 1 through 12 of 12 returned.

☐ 1. Document ID: US 4798786 A

L6: Entry 1 of 12

File: USPT

Jan 17, 1989

US-PAT-NO: 4798786

DOCUMENT-IDENTIFIER: US 4798786 A

TITLE: Living cells encapsulated in crosslinked protein

DATE-ISSUED: January 17, 1989

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|--------------------|------------|-------|----------|---------|
| Tice; Thomas R. | Birmingham | AL | | |
| Meyers; William E. | Helena | AL | | |

US-CL-CURRENT: [435/177](#); [435/178](#), [435/182](#), [435/252.1](#), [435/382](#)

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|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|------|---------|
| Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | RMIC | Draw D. |
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|------|---------|

☐ 2. Document ID: US 3812151 A

L6: Entry 2 of 12

File: USOC

May 21, 1974

US-PAT-NO: 3812151

DOCUMENT-IDENTIFIER: US 3812151 A

TITLE: BETA- (2,4,6-TRIIODO-3-ACETAMIDINOPHENYL) -PROPIONIC ACIDS

DATE-ISSUED: May 21, 1974

INVENTOR-NAME: HARWART A; SCHULZE P ; KOLB K ; PFEIFFER H

US-CL-CURRENT: [548/569](#), [540/450](#), [540/610](#), [544/165](#), [544/399](#), [546/235](#), [548/967](#),
[562/440](#)

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|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|------|---------|
| Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | RMIC | Draw D. |
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|------|---------|

☐ 3. Document ID: US 3745161 A

L6: Entry 3 of 12

File: USOC

Jul 10, 1973

US-PAT-NO: 3745161

DOCUMENT-IDENTIFIER: US 3745161 A

TITLE: PHENYL-HYDROXY-PYRAZINE CARBOXYLIC ACIDS AND DERIVATIVES

DATE-ISSUED: July 10, 1973

INVENTOR-NAME: WALFORD G; SHEN T ; WITZEL B

US-CL-CURRENT: 544/406, 514/870, 540/601, 544/225, 544/295, 544/298, 544/319,
544/357, 544/405, 544/407

| Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | RMK | Draw D. |
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|-----|---------|
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☐ 4. Document ID: US 3720675 A

L6: Entry 4 of 12

File: USOC

Mar 13, 1973

US-PAT-NO: 3720675

DOCUMENT-IDENTIFIER: US 3720675 A

TITLE: PYRAZOLO(3,4-B)PYRIDINE-5-CARBOXAMIDES

DATE-ISSUED: March 13, 1973

INVENTOR-NAME: BERNSTEIN J; HOEHN H

US-CL-CURRENT: 544/362, 540/575, 540/597, 544/127, 544/229, 544/58.4, 546/120

| Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | RMK | Draw D. |
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|-----|---------|
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☐ 5. Document ID: US 3660403 A

L6: Entry 5 of 12

File: USOC

May 2, 1972

US-PAT-NO: 3660403

DOCUMENT-IDENTIFIER: US 3660403 A

TITLE: HALOPHENYLPYRIMIDINE CARBOXYLIC ACIDS

DATE-ISSUED: May 2, 1972

INVENTOR-NAME: SHEN TSUNG-YING; WITZEL BRUCE E ; WALFORD GORDON L

US-CL-CURRENT: 544/298, 514/825, 514/870, 544/295, 544/319

| Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | RMIC | Draw D. |
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|------|---------|
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|------|---------|

☐ 6. Document ID: US 3562277 A

L6: Entry 6 of 12

File: USOC

Feb 9, 1971

US-PAT-NO: 3562277

DOCUMENT-IDENTIFIER: US 3562277 A

TITLE: KETONIC DERIVATIVES OF PHENYL PIPERAZINES

DATE-ISSUED: February 9, 1971

INVENTOR-NAME: CINNAMON JEROME MARSHALL; HANSEN HOLGER VICTOR ; OROSHNIK WILLIAM

US-CL-CURRENT: 544/394, 544/377, 549/436, 568/306, 568/316, 568/335, 568/337

| Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | RMIC | Draw D. |
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|------|---------|
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|------|---------|

☐ 7. Document ID: US 3557094 A

L6: Entry 7 of 12

File: USOC

Jan 19, 1971

US-PAT-NO: 3557094

DOCUMENT-IDENTIFIER: US 3557094 A

TITLE: SUBSTITUTED ALKYL ESTERS OF ALPHA-CARBOXY ARYL PENICILLINS

DATE-ISSUED: January 19, 1971

INVENTOR-NAME: BUTLER KENNETH

US-CL-CURRENT: 540/338

| Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | RMIC | Draw D. |
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|------|---------|
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|------|---------|

☐ 8. Document ID: US 3492380 A

L6: Entry 8 of 12

File: USOC

Jan 27, 1970

US-PAT-NO: 3492380

DOCUMENT-IDENTIFIER: US 3492380 A

TITLE: PROCESS FOR ENCAPSULATION

DATE-ISSUED: January 27, 1970

INVENTOR-NAME: SANTO JOHN EUGENE; VANDEGAER JAN EDMOND

US-CL-CURRENT: 264/4, 264/4.7, 264/7, 264/9, 424/419, 427/213.3, 428/402.24

| Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | RMK | Draw D. |
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|-----|---------|
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☐ 9. Document ID: US 3470171 A

L6: Entry 9 of 12

File: USOC

Sep 30, 1969

US-PAT-NO: 3470171

DOCUMENT-IDENTIFIER: US 3470171 A

TITLE: OXAZINOISOQUINOLINE DERIVATIVES

DATE-ISSUED: September 30, 1969

INVENTOR-NAME: CLARKE FRANK H JR

US-CL-CURRENT: 544/73; 250/396R, 514/906, 544/101, 544/148, 544/163, 544/169,
544/99, 549/437, 549/441, 549/442, 558/390 , 564/165

| Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | RMK | Draw D. |
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|-----|---------|
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☐ 10. Document ID: US 3069432 A

L6: Entry 10 of 12

File: USOC

Dec 18, 1962

US-PAT-NO: 3069432

DOCUMENT-IDENTIFIER: US 3069432 A

TITLE: 5-(aminoalkyl)-5, 11-dihydrodibenzo-oxazepines

DATE-ISSUED: December 18, 1962

INVENTOR-NAME: LOUIS YALE HARRY; ALEXANDER SOWINSKI FRANCIS ; JACK BERNSTEIN

US-CL-CURRENT: 540/550, 250/396R, 544/60, 564/219, 564/443, 564/90

| Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | RMK | Draw D. |
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|-----|---------|
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|-----|---------|

☐ 11. Document ID: US 2855401 A

L6: Entry 11 of 12

File: USOC

Oct 7, 1958

US-PAT-NO: 2855401

DOCUMENT-IDENTIFIER: US 2855401 A

TITLE: Certain n-(aminophenoxy pentyl) sulfonamide or saccharine compounds and
higher homologues

DATE-ISSUED: October 7, 1958

INVENTOR-NAME: JAMES BARBER HARRY; FREDERICK COLLINS RAYMOND ; MICHAEL DAVIS

US-CL-CURRENT: 548/210, 564/93, 564/99

| | | | | | | | | | | | | |
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|------|----------|
| Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | FIGS | Drawings |
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|------|----------|

☐ 12. Document ID: US 2125221 A

L6: Entry 12 of 12

File: USOC

Jul 26, 1938

US-PAT-NO: 2125221

DOCUMENT-IDENTIFIER: US 2125221 A

TITLE: Blasting cap

DATE-ISSUED: July 26, 1938

INVENTOR-NAME: COX RICHARD F B

US-CL-CURRENT: 102/275.9; 149/15, 149/80, 564/107, 564/370

| | | | | | | | | | | | | |
|------|-------|----------|-------|--------|----------------|------|-----------|--|--|--------|------|----------|
| Full | Title | Citation | Front | Review | Classification | Date | Reference | | | Claims | FIGS | Drawings |
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cox\$2 same (ethanolamine or \$diamine or amino
or benethamine or benzathine or piperazine or
hydrabamine or imidazole) same capsule

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L8: Entry 38 of 136

File: PGPB

Nov 11, 2004

DOCUMENT-IDENTIFIER: US 20040224020 A1

TITLE: Oral dosage forms with therapeutically active agents in controlled release cores and immediate release gelatin capsule coats

Detail Description Paragraph:

[0121] An oral dosage form according to the invention of the controlled release core and/or immediate release gelatin capsule may further include, in addition to a therapeutically active agent, including, for example, an opioid agonist and optionally an opioid antagonist, one or more drugs that may or may not act synergistically with such agent(s). For example, a combination of two opioid agonists may be included in the dosage form, in addition to the opioid antagonist. For example, the dosage form may include two opioid agonists having different properties, such as half-life, solubility, potency, and a combination of any of the foregoing. Alternatively, one or more opioid agonists are included and a non-opioid drug is also included, alternatively or in addition to an opioid antagonist. However, non-opioid drugs can provide additional analgesia, and include, for example, aspirin, acetaminophen; non-steroidal anti-inflammatory drugs ("NSAIDS"), e.g., ibuprofen, ketoprofen, etc.; N-methyl-D-aspartate (NMDA) receptor antagonists, e.g., a morphinan such as dextromethorphan or dextrorphan, or ketamine; cyclooxygenase-II inhibitors ("COX II inhibitors") ; cyclooxygenase-III inhibitors ("COX-III inhibitors") and/or glycine receptor antagonists.

Detail Description Paragraph:

[0135] At least one therapeutically active agent in the immediate release gelatin capsule coating and/or at least one therapeutically active agent in the controlled release core of the present invention may be provided in the form of free bases or pharmaceutically acceptable acid addition salts. Pharmaceutically acceptable salts refer to derivatives of a therapeutically active agent, wherein the therapeutically active agent is modified by making an acid or base salts thereof. The pharmaceutically acceptable salt embraces an inorganic or an organic salt. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of the therapeutically active agent. Non-limiting examples of pharmaceutically acceptable salts include, but are not limited to, metal salts such as sodium, potassium salt, sodium salt and the like; alkaline earth metals such as calcium salt, magnesium salt and the like; organic amine salts such as triethylamine salt, pyridine salt, picoline salt, ethanolamine salt, triethanolamine salt, dicyclohexylamine salt, N,N'-dibenzylethylenediamine salt and the like; inorganic acid salts such as hydrochloride, hydrobromide, sulfate, phosphate and the like; organic acid salts such as formate, acetate, trifluoroacetate, maleate, tartarate and the like; sulfonates such as methanesulfonate, benzenesulfonate, p-toluenesulfonate, and the like; amino acid salts such as arginate, aspartate, glutamate and the like. The pharmaceutically acceptable salts include the conventional non-toxic salts made, for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include those derived from inorganic acids such as hydrochloric, hydrobromic, sulfuric, sulfonic, sulfamic, phosphoric, nitric and others known to those skilled in the art; and the salts prepared from organic acids such as amino acids, acetic, propionic, succinic, glycolic, stearic, lactic, malic, malonic, tartaric, citric, ascorbic, pantoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic,

ethane disulfonic, oxalic, isethionic, glucuronic, and other acids. Other pharmaceutically acceptable salts and variants include mucates, phosphate (dibasic), phosphate (monobasic), acetate trihydrate, bi(heptafluorobutyrate), bi(methylcarbamate), bi(pentafluoropropionate), mesylate, bi(pyridine-3-carboxylate), bi(trifluoroacetate), bitartrate, chlorhydrate, and sulfate pentahydrate. An oxide, though not usually referred to by chemists as a salt, is also a "pharmaceutically acceptable salt" for the present purpose. For acidic compounds, the salt may include an amine-based (primary, secondary, tertiary or quaternary amine) counter ion, an alkali metal cation, or a metal cation. Lists of suitable salts are found in texts such as Remington's Pharmaceutical Sciences, 18.sup.th Ed. (Alfonso R. Gennaro, ed.; Mack Publishing Company, Easton, Pa., 1990); Remington: the Science and Practice of Pharmacy 19.sup.th Ed. (Lippincott, Williams & Wilkins, 1995); Handbook of Pharmaceutical Excipients, (Arthur H. Kibbe, ed.; Amer. Pharmaceutical Assoc., 2002); the Pharmaceutical Codex: Principles and Practice of Pharmaceutics 12.sup.th Ed. (Walter Lund ed.; Pharmaceutical Press, London, 1994); The United States Pharmacopeia: The National Formulary (United States Pharmacopeial Convention); and Goodman and Gilman's: The Pharmacological Basis of Therapeutics 10.sup.th Ed. (Louis S. Goodman and Lee E. Limbird, eds.; McGraw Hill, 2002), the disclosures of which are hereby incorporated by reference.

Detail Description Paragraph:

[0141] Acidifying agents include compounds used to provide an acidic medium for product stability. Such compounds include, by way of example and without limitation, acetic acid, amino acid, citric acid, fumaric acid and other alpha hydroxy acids, hydrochloric acid, ascorbic acid, nitric acid, phosphoric acid, and others known in the art.

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L8: Entry 43 of 136

File: PGPB

Oct 14, 2004

DOCUMENT-IDENTIFIER: US 20040204413 A1

TITLE: Pharmaceutical compositions containing a COX-II inhibitor and a muscle relaxant

Summary of Invention Paragraph:

[0010] Specific embodiments of the invention include those wherein: 1) the pharmaceutical composition is contained within a dosage form such as a gel, cream, ointment, pill, tablet, capsule, liquid, suspension, osmotic device, bead, granule, spheroid, particulate, paste, prill, reconstitutable solid, powder, or injectible liquid; 2) the pharmaceutical composition is adapted for oral, buccal, ocular, otic, dermal, rectal, vaginal, parenteral, sublingual, nasal, or pulmonary delivery; 3) the muscle relaxant is selected from the group consisting of alcuronium, alosetron, aminophylline, baclofen, carisoprodol (SOMA.RTM.), chlorphenesin, chlorphenesin carbamate, chlorzoxazone (PARAFON FORTES), chlormezanone, cyclobenzaprine (FLEXERIL.RTM.), dantrolene, decamethonium, diazepam, dyphylline, eperisone, ethaverine, gallamine triethiodide, hexafluorenum, mephenesin, metaxalone (SKELAXIN.RTM.), methocarbamol (ROBAXIN.RTM.), metocurine iodide, orphenadrine (NORFLEX.RTM.), pancuronium, papaverine, pipercuronium, pridinol (pridinolum), succinylcholine, theophylline, tizanidine, tolperisone, tubocurarine, vecuronium, idrocilamide, ligustilide, cnidilide, and senkyunolide; 4) the pharmaceutical composition is a solid dosage form that independently provides a controlled, delayed, sustained, immediate, timed, slow or rapid release of each of the COX-II inhibitor and the muscle relaxant; 5) the pharmaceutical composition provides therapeutically effective plasma levels of the COX-II inhibitor and muscle relaxant for a period of at least 12 hours after administration; and/or 6) the COX-II inhibitor is selected from the group consisting of rofecoxib (VIOXX.TM., MK-0966), celecoxib (CELEBREX.TM., SC-58635), flosulide (CGP-28238), NS-398, DUP-697, meloxicam, 6-methoxy-2-naphthylacetic acid (6-MNA), nabumetone (prodrug for 6-MNA), etodolac, nimesulide, SC-5766, SC-58215, T-614 and combinations thereof.

Detail Description Paragraph:

[0032] In one embodiment, the COX-II inhibitor and the muscle relaxant are released concurrently. This type of release occurs when the two drugs are included together in admixture, for example, in a tablet core, powder, capsule, bead, granule, liquid, paste, gel, cream, ointment, patch, implant and other similar dosage forms capable of simultaneously delivering two or more drugs.

Detail Description Paragraph:

[0033] In another embodiment, the COX-II inhibitor and the muscle relaxant are released sequentially. This type of release occurs when the first drug is included in one part of a dosage form and the second drug is included in another part of the same dosage form, and release of the second drug begins shortly after or nearly at the end of completion of release of the first drug. Such dosage form would include those wherein the first drug is included in a core and the second drug is included in a coat surrounding the core, a bilayered tablet with each drug being in a different core, a dosage form providing a rapid release of the first drug and a controlled release of the second drug. Suitable dosage forms for this embodiment include, for example, a layered patch, layered or coated tablet or bead, layered or coated osmotic device, capsule containing a mixture of beads that provide different

release profiles for the drugs, and layered or coated implant.

Detail Description Paragraph:

[0034] In yet another embodiment, the COX-II inhibitor and the muscle relaxant are released in spaced apart periods of time. This type of release occurs when the first drug is released during a first period of time and the second drug is released during a later second period of time. Dosage forms suitable for this type of release are generally considered targeted, enteric or timed-release dosage forms. Suitable dosage forms for this embodiment include, for example, a layered patch, layered or coated tablet, layered or coated osmotic device, capsule containing a mixture of beads that provide different release profiles for the drugs, and layered or coated implant.

Detail Description Paragraph:

[0039] The COX-II inhibitor and muscle relaxant are independently used in their free acid, free base or pharmaceutically acceptable salt forms. When mentioned herein, the COX-II inhibitor and muscle relaxant are taken to be independently present in their free and/or salt forms. As used herein, "pharmaceutically acceptable salts" refer to derivatives of the disclosed compounds wherein the therapeutic compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of the COX-II inhibitor or muscle relaxant. The pharmaceutically acceptable salts include the conventional non-toxic salts, for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include those derived from inorganic acids such as hydrochloric, hydrobromic, sulfuric, sulfonic, sulfamic, phosphoric, nitric and others known to those of ordinary skill in the art; and the salts prepared from organic acids such as amino acids, acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, pantoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isethionic, and other known to those of ordinary skill in the pharmaceutical sciences. For acidic compounds, the salt may include an amine-based (primary, secondary, tertiary or quaternary amine) counter ion, an alkali metal cation, or a metal cation. Lists of suitable salts are found in texts such as Remington's Pharmaceutical Sciences, 18th Ed. (Alfonso R. Gennaro, ed.; Mack Publishing Company, Easton, Pa., 1990); Remington: the Science and Practice of Pharmacy 19th Ed. (Lippincott, Williams & Wilkins, 1995); Handbook of Pharmaceutical Excipients, 3rd Ed. (Arthur H. Kibbe, ed.; Amer. Pharmaceutical Assoc., 1999); the Pharmaceutical Codex: Principles and Practice of Pharmaceutics 12th Ed. (Walter Lund ed.; Pharmaceutical Press, London, 1994); The United States Pharmacopoeia: The National Formulary (United States Pharmacopoeial Convention); and Goodman and Gilman's: the Pharmacological Basis of Therapeutics (Louis S. Goodman and Lee E. Limbird, eds.; McGraw Hill, 1992), the disclosures of which are hereby incorporated by reference.

Detail Description Paragraph:

[0069] As used herein, the term "acidifying agent" is intended to mean a compound used to provide an acidic medium for product stability. Such compounds include, by way of example and without limitation, acetic acid, amino acid, citric acid, fumaric acid and other alpha hydroxy acids, such as hydrochloric acid, ascorbic acid, and nitric acid and others known to those of ordinary skill in the art.

Detail Description Paragraph:

[0131] The following general composition is used to prepare immediate release capsules that provide an immediate release of a COX-II inhibitor and a muscle relaxant. This dosage form is used for oral administration for the treatment of pain. The following ingredients are used in the approximate amounts indicated.

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L8: Entry 118 of 136

File: USPT

Sep 2, 2003

US-PAT-NO: 6613354

DOCUMENT-IDENTIFIER: US 6613354 B2

TITLE: Oral pharmaceutical dosage forms comprising a proton pump inhibitor and a NSAID

DATE-ISSUED: September 2, 2003

INVENTOR-INFORMATION:

| NAME | CITY | STATE | ZIP CODE | COUNTRY |
|---------------|----------|-------|----------|---------|
| Depui; Helene | Goteborg | | | SE |
| Lundberg; Per | Molndal | | | SE |

US-CL-CURRENT: [424/458](#); [424/451](#), [424/452](#), [424/457](#)

CLAIMS:

What is claimed is:

1. A capsule formulation comprising an acid susceptible proton pump inhibitor, one or more Non Steroidal Antiinflammatory Drugs (NSAID(s)), an enteric coating layer to protect the proton pump inhibitor and, optionally, pharmaceutically acceptable excipients.
2. The capsule formulation according to claim 1, wherein the proton pump inhibitor is in the form of pellets covered with an enteric coating layer.
3. The capsule formulation according to claim 1, further comprising a separating layer located underneath the enteric coating layer.
4. The capsule formulation according to claim 1, wherein the dosage form comprises the proton pump inhibitor and one NSAID.
5. The capsule formulation according to claim 1, wherein the proton pump inhibitor is omeprazole, an alkaline salt of omeprazole, a single enantiomer of omeprazole or an alkaline salt of the single enantiomer.
6. The capsule formulation according to claim 5, wherein the proton pump inhibitor is S-omeprazole magnesium salt.
7. The capsule formulation according to claim 1, wherein the proton pump inhibitor is lansoprazole, a pharmaceutically acceptable salt of lansoprazole, a single enantiomer of lansoprazole or a pharmaceutically acceptable salt of the single enantiomer.
8. The capsule formulation according to claim 1, wherein the proton pump inhibitor is pantoprazole, a pharmaceutically acceptable salt of pantoprazole,

a single enantiomer of pantoprazole or a pharmaceutically acceptable salt of the single enantiomer.

9. The capsule formulation according to any one of claims 5-8, wherein the NSAID(s) is selected from the group consisting of ibuprofen, diclofenac, piroxicam, naproxen and pharmaceutical acceptable salts thereof.

10. The capsule formulation according to any one of claims 5-8, wherein the NSAID is diclofenac or piroxicam, or pharmaceutically acceptable salt thereof.

11. The capsule formulation according to claim 1, wherein the amount of the proton pump inhibitor is in the range of 10-80 mg and the amount of NSAID(s) is in the range of 10-800 mg.

12. The capsule formulation according to claim 1, wherein the amount of the proton pump inhibitor is in the range of 10-40 mg and the amount of NSAID(s) is in the range of 10-500 mg.

13. The capsule formulation according to claim 2, wherein the acid resistance of the enteric coating layered pellets is in compliance with the requirements on enteric coating layered articles defined in the United States Pharmacopeia.

14. The capsule formulation according to claim 2, wherein the acid resistance of the enteric coating layered pellets does not decrease more than 10% in compliance with the requirements on enteric coating layered articles defined in the United States Pharmacopeia.

15. The capsule formulation according to claim 2, wherein the enteric coating of the individual pellets comprises a plasticizer.

16. The capsule formulation according to claim 2, wherein the enteric coating layered pellets are further covered with an over-coating layer comprising pharmaceutically acceptable excipients.

17. The capsule formulation according to claim 1, wherein the proton pump inhibitor is in the form of pellets covered with an enteric coating layer, and wherein the NSAID(s), is in the form of pellets covered with an enteric coating layer.

18. The capsule formulation according to claim 1, wherein the proton pump inhibitor is in the form of pellets covered with an enteric coating layer, and wherein the NSAID(s) is in the form of pellets coating layered with an extended release film.

19. A process for the manufacture of a capsule formulation comprising a proton pump inhibitor and one or more Non Steroidal Antiinflammatory Drugs (NSAID(s)), wherein the process comprises the steps: (a) preparing the proton pump inhibitor in the form of enteric coating layered pellets, and (b) filling a capsule with the pellets, the NSAID(s) selected from the group consisting of prepared NSAID granules, enteric coating layered NSAID pellets, and NSAID pellets coating layered with an extended release film, and optionally, pharmaceutically acceptable excipients.

20. A method for the treatment of gastrointestinal side-effects associated with NSAID treatment in mammals and man by administering to a host in need thereof a therapeutically effective dose of the capsule formulation according to any one of claims 1-8, or 11-18.

21. The method according to claim 20, wherein the disorder is an upper gastrointestinal disorder associated with NSAID treatment.

22. The capsule formulation according to any one of claims 5-8, wherein the NSAID is a NO-releasing NSAID, salt, hydrate, or ester thereof.

23. The capsule formulation according to claim 22, wherein the NO-releasing NSAID is selected from the group consisting of NO-releasing diclofenac and NO-releasing naproxen.

24. The capsule formulation according to one of claims 5-8, wherein the NSAID is a (COX)2 selective NSAID, salt, hydrate or ester thereof.

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| <u>L7</u> | cox\$2 same capsule | 365 | <u>L7</u> |
| <u>L6</u> | cox\$2 same (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) same capsule | 12 | <u>L6</u> |
| <u>L5</u> | cox\$ same (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) same capsule same (stabiliz\$ or cross\$) | 3 | <u>L5</u> |
| <u>L4</u> | L3 and cyclooxygenase\$ | 19 | <u>L4</u> |
| <u>L3</u> | (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) same capsule same (stabiliz\$ or cross\$) | 895 | <u>L3</u> |
| <u>L2</u> | (celecoxib or deracoxib or valdecoxib or rofecoxib or etoricoxib) same (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) and capsule | 261 | <u>L2</u> |

L1 (celecoxib or deracoxib or valdecoxib or rofecoxib or etoricoxib) same
(ethanolamine or \$diamine or amino or benethamine or benzathine or
piperazine or hydrabamine or imidazole) same capsule

12 L1

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L9: Entry 32 of 40

File: PGPB

Jun 20, 2002

DOCUMENT-IDENTIFIER: US 20020077328 A1

TITLE: Selective cyclooxygenase-2 inhibitors and vasomodulator compounds for generalized pain and headache pain

Detail Description Paragraph:

[0320] A composition of the present invention optionally comprises at least one pharmaceutically acceptable free radical-scavenging antioxidant. Non-limiting illustrative examples of suitable free radical-scavenging antioxidants include alpha-tocopherol (vitamin E), ascorbic acid (vitamin C) and salts thereof including sodium ascorbate and ascorbic acid palmitate, butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), fumaric acid and salts thereof, hypophosphorous acid, malic acid, alkyl gallates, for example propyl gallate, octyl gallate and lauryl gallate, sodium sulfite, sodium bisulfite and sodium metabisulfite. Preferred free radical-scavenging antioxidants are alkyl gallates, vitamin E, BHA and BHT. More preferably the at least one free radical-scavenging antioxidant is propyl gallate.

Detail Description Table CWU:

3TABLE 3 Possible components of Drug Substance Selective cyclooxy- Rapid Forms of
genase-2 Vasomodul- Onset Drug Inhibitor ator Vehicle Substance Excipients Any
vasomodul- concen- Discrete free- selective ator trated dose radical COX-2 solution
scavenging described idant in Section I. above vasocon- solution/ Imbibable fatty
strictor suspension liquid acid- organic amine pair vasodila- amorphous Tablet
crystalli- tor component zation inhibitor xanthine nanopart- Capsule wetting
iculate agent component caffeine micropart- Suspension diluent iculate component
dual Sterile disinte- release aqueous grant/eff- solution ervescent agent gels,
binding vreams, agent/ad- oils hesive Supposi- lubricant tory Lozenges co-solvent
sweetener preserva- tive dispersant emulsify- ing agent buffering agent flavoring
agent colorant stabilizer thickener

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| <u>L9</u> L7 and sulfite | 40 | <u>L9</u> |
| <u>L8</u> L7 and (amino adj1 acid) | 136 | <u>L8</u> |
| <u>L7</u> cox\$2 same capsule | 365 | <u>L7</u> |
| <u>L6</u> cox\$2 same (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) same capsule | 12 | <u>L6</u> |
| <u>L5</u> cox\$ same (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) same capsule same (stabiliz\$ or cross\$) | 3 | <u>L5</u> |
| <u>L4</u> L3 and cyclooxygenase\$ | 19 | <u>L4</u> |
| <u>L3</u> (ethanolamine or \$diamine or amino or benethamine or benzathine or piperazine or hydrabamine or imidazole) same capsule same (stabiliz\$ or cross\$) | 895 | <u>L3</u> |
| <u>L2</u> (celecoxib or deracoxib or valdecoxib or rofecoxib or etoricoxib) same (ethanolamine or \$diamine or amino or benethamine or benzathine or | 261 | <u>L2</u> |

piperazine or hydrabamine or imidazole) and capsule
(celecoxib or deracoxib or valdecoxib or rofecoxib or etoricoxib) same
L1 (ethanolamine or \$diamine or amino or benethamine or benzathine or
piperazine or hydrabamine or imidazole) same capsule

12 L1

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L8: Entry 128 of 136

File: USPT

Apr 10, 2001

DOCUMENT-IDENTIFIER: US 6214378 B1

TITLE: Capsules for oral preparations and capsule preparations for oral administration

Drawing Description Text (14):

Incidentally, with regard to an anti-inflammatory agent, a cyclooxygenase (COX)-2 inhibitor is preferred. In addition, the pharmacologically active substance to be encapsulated in the capsule as well as the composition consisting of that and the following various additives to be added thereto are to be usually in a neutral or alkaline region of around pH 7 or, preferably, lower than that. If necessary, additives such as vehicle, liquid agent, absorbefacient and others for various purposes may be compounded in the capsule. The vehicle at that time is appropriately selected from lactose, starch, talc, lactose, calcium hydrogen phosphate, sodium hydrogen phosphate, synthetic aluminum silicate, magnesium metasilicate aluminate, aluminum magnesium hydroxide, synthetic hydrotalcite, magnesium silicate, natural aluminum silicate, potassium carbonate, calcium carbonate, sodium carbonate, magnesium oxide, magnesium carbonate, sodium hydrogen carbonate, potassium hydrogen carbonate, silicic acid anhydride, light silicic acid anhydride, sodium hydroxide, tetrasodium pyrophosphate, anhydrous sodium pyrophosphate, anhydrous trisodium phosphate, dipotassium phosphate, anhydrous sodium sulfite, sodium ditartrate, etc. Incidentally, in adjusting the pH of the pharmaceutical-containing composition in the capsules, the adjustment may be conducted by selecting from those vehicles if necessary.

Drawing Description Text (15):

In the case of a liquid preparation, the use of glycerol, soybean oil, polyethylene glycol 400 (PEG 400), docosahexaenoic acid, eicosapentaenoic acid, pirotiodecane (chemical name: 1-[2-(decylthio)ethyl]azacyclopentan-2-one), sesame oil, safflower oil, cotton seed oil and olive oil may be exemplified. Further, with an object of accelerating the absorption of the pharmacologically active substance, absorbefacient such as sucrose fatty acid ester, glycyrrhizinate, glycyrrhetinic acid, bile acid and conjugated compound thereof, pirotiodecane, glycerol fatty acid ester, adipic acid, basic amino acid, polyethylene glycol, sodium caprate, sodium dodecyl sulfate and sodium deoxycholate may be added.

CLAIMS:

12. The capsule preparation according to claim 11, wherein the absorbefacient is selected from a group consisting of sucrose fatty acid ester, glycyrrhizinate, glycyrrhetinic acid, bile acid and conjugated compound thereof, pirotiodecane, glycerol fatty acid ester, adipic acid, basic amino acid, polyethylene glycol, sodium caprate, sodium dodecyl sulfate and sodium deoxycholate.

24. The method according to claim 23, wherein the absorbefacient is selected from the group consisting of sucrose fatty acid ester, glycyrrhizinate, glycyrrhetinic acid, bile acid and conjugated compound thereof, pirotiodecane, glycerol fatty acid ester, adipic acid, basic amino acid, polyethylene glycol, sodium caprate, sodium dodecyl sulfate and sodium deoxycholate.

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L1: Entry 60 of 89

File: PGPB

Aug 8, 2002

DOCUMENT-IDENTIFIER: US 20020107250 A1

TITLE: Rapid-onset formulation of a selective cyclooxygenase-2 inhibitor

Summary of Invention Paragraph:

[0023] Many selective COX-2 inhibitory compounds, including celecoxib, deracoxib, valdecoxib, rofecoxib and etoricoxib, have low solubility in aqueous media. In addition, some, for example celecoxib, have relatively high dose requirements. These properties present practical problems in formulating concentrated solutions of selective COX-2 inhibitory drugs for rapid-onset, oral administration. With respect to such high dose, low solubility drugs, the size of the gelatin capsule or volume of solution required to provide a therapeutic dose becomes a limiting factor. For example, a drug that has a solubility of 10 mg/ml in a given solvent and a therapeutic dose of 400 mg/day would require ingestion of 40 ml of solution. Such a volume is inconvenient or unacceptable for consumption in imbibable form; this volume also presents particular problems where a discrete dosage form is desired because capsules that contain more than about 1.0 ml to about 1.5 ml of liquid are generally considered to be too large for comfortable consumption. Alternatively, multiple capsules would need to be ingested in order to get the required dose.

Detail Description Paragraph:

[0242] Compositions of the invention can be prepared by any suitable method of pharmacy that includes the step of bringing into association the selective COX-2 inhibitory drug and the solvent liquid. In general, celecoxib compositions are prepared by uniformly and intimately admixing celecoxib with a solvent liquid and then, if desired, encapsulating the resulting solution or solution/suspension, preferably in a soft gelatin capsule. Encapsulation can be performed by any method known in the art including, but not limited to, the plate process and the rotary die process as described, for example, by Ansel et al. (1995) in *Pharmaceutical Dosage Forms and Drug Delivery Systems*, 6th ed., Williams & Wilkins, Baltimore, Md., pp. 176-182.

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L1: Entry 63 of 89

File: PGPB

Feb 7, 2002

DOCUMENT-IDENTIFIER: US 20020016342 A1

TITLE: Combination therapy using COX-2 selective inhibitor and thromboxane inhibitor and compositions therefor

Detail Description Table CWU:

4 Ingredient Amount per capsule COX-2 Selective Inhibitor 25 mg Microcrystalline cellulose 37 mg Lactose anhydrate 37 mg Magnesium stearate 1 mg Hard gelatin capsule 1 capsule

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L1: Entry 75 of 89

File: USPT

Apr 22, 2003

DOCUMENT-IDENTIFIER: US 6552031 B1

**** See image for Certificate of Correction ****

TITLE: Synergistic analgesic combination of oxycodone and rofecoxib

Detailed Description Text (26):

The combination of COX-2 inhibitor and an opioid analgesic can be employed in admixtures with conventional excipients, i.e., pharmaceutically acceptable organic or inorganic carrier substances suitable for oral, parenteral, nasal, intravenous, subcutaneous, enteral, or any other suitable mode of administration, known to the art. Suitable pharmaceutically acceptable carriers include but are not limited to water, salt solutions, alcohols, gum arabic, vegetable oils, benzyl alcohols, polyethylene glycols, gelate, carbohydrates such as lactose, amylose or starch, magnesium stearate talc, silicic acid, viscous paraffin, perfume oil, fatty acid monoglycerides and diglycerides, pentaerythritol fatty acid esters, hydroxymethylcellulose, polyvinylpyrrolidone, etc. The pharmaceutical preparations can be sterilized and if desired mixed with auxiliary agents, e.g., lubricants, preservatives, stabilizers, wetting agents, emulsifiers, salts for influencing osmotic pressure buffers, coloring, flavoring and/or aromatic substances and the like. They can also be combined where desired with other active agents, e.g., other analgesic agents. For parenteral application, particularly suitable are oily or aqueous solutions, as well as suspensions, emulsions, or implants, including suppositories. Ampoules are convenient unit dosages. For oral application, particularly suitable are tablets, dragees, liquids, drops, suppositories, or capsules, caplets and gelcaps. The compositions intended for oral use may be prepared according to any method known in the art and such compositions may contain one or more agents selected from the group consisting of inert, non-toxic pharmaceutically excipients which are suitable for the manufacture of tablets. Such excipients include, for example an inert diluent such as lactose; granulating and disintegrating agents such as cornstarch; binding agents such as starch; and lubricating agents such as magnesium stearate. The tablets may be uncoated or they may be coated by known techniques for elegance or to delay release of the active ingredients. Formulations for oral use may also be presented as hard gelatin capsules wherein the active ingredient is mixed with an inert diluent.

Detailed Description Text (31):

The sustained release dosage form may include the opioid analgesic in sustained release form and COX-2 inhibitor in sustained release form or in immediate release form. The COX-2 inhibitor may be incorporated into the sustained release matrix along with the opioid; incorporated into the sustained release coating; incorporated as a separated sustained release layer or immediate release layer; or may be incorporated as a powder, granulation, etc., in a gelatin capsule with the substrates of the present invention. Alternatively, the sustained release dosage form may have the COX-2 inhibitor in sustained release form and the opioid analgesic in sustained release form or immediate release form.

Detailed Description Text (34):

In certain embodiments, the particles comprise normal release matrixes containing the opioid analgesic with or without the COX-2 inhibitor. These particles are then coated with the sustained release carrier in embodiments where the COX-2 inhibitor is immediately released, the COX-2 inhibitor may be included in separate normal

release matrix particles, or may be co-administered in a different immediate release composition which is either enveloped within a gelatin capsule or is administered separately. In other embodiments, the particles comprise inert beads which are coated with the opioid analgesic with or without the COX-2 inhibitor. Thereafter, a coating comprising the sustained release carrier is applied onto the beads as an overcoat.

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L1: Entry 77 of 89

File: USPT

Aug 27, 2002

DOCUMENT-IDENTIFIER: US 6440967 B1

TITLE: Combination of a GABAA alpha 5 inverse agonist and COX-2 inhibitor, NSAID, estrogen or vitamin E

Detailed Description Paragraph Table (5):

Hard gelatin capsule composition Amount (mg) per capsule COX-2 Inhibitor 25
Microcrystalline cellulose 37 Lactose anhydrate 37 Magnesium stearate 1 Hard
gelatin capsule 1 capsule

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File: USPT

May 16, 2000

DOCUMENT-IDENTIFIER: US 6063811 A

**** See image for [Certificate of Correction](#) ****

TITLE: Compositions for a once day treatment of cyclooxygenase-2 mediated diseases

Detailed Description Paragraph Table (9):

| | Hard <u>gelatin capsule</u> composition | Amount per capsule |
|-------------------------------|---|------------------------------|
| Ingredient | | 25 mg <u>COX-2</u> Inhibitor |
| mg Microcrystalline cellulose | 37 mg | Lactose anhydrate |
| 1 mg | Magnesium stearate | 1 capsule |
| Hard <u>gelatin capsule</u> | | |

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| cross\$link\$ adj5 (gelatin adj3 capsule) | 45 |

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| <u>L13</u> | cross\$link\$ (gelatin adj3 capsule) | 469133 | <u>L13</u> |
| <u>L12</u> | L9 and free adj1 radical | 6 | <u>L12</u> |
| <u>L11</u> | L10 and \$sulfite | 0 | <u>L11</u> |
| <u>L10</u> | L9 and free\$radical | 0 | <u>L10</u> |
| <u>L9</u> | cross\$ adj5 (gelatin adj3 capsule) | 48 | <u>L9</u> |
| <u>L8</u> | \$sulfite adj10 inhibit\$ adj10 \$aldehyde | 6 | <u>L8</u> |
| <u>L7</u> | \$sulfite adj5 inhibit\$ adj5 \$aldehyde | 3 | <u>L7</u> |
| <u>L6</u> | \$sulfite adj5 (gelatin adj3 capsule) | 7 | <u>L6</u> |
| <u>L5</u> | L4 and 424/\$.ccls. | 18 | <u>L5</u> |
| <u>L4</u> | \$sulfite adj5 \$aldehyde | 997 | <u>L4</u> |
| <u>L3</u> | L1 and 424/\$.ccls. | 4 | <u>L3</u> |
| <u>L2</u> | L1 and (gelatin adj3 capsule) | 4 | <u>L2</u> |
| <u>L1</u> | sulfite adj5 \$aldehyde | 494 | <u>L1</u> |

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L14: Entry 27 of 45

File: USPT

Feb 23, 1999

DOCUMENT-IDENTIFIER: US 5874106 A

TITLE: Filled gelatin capsules

Abstract Text (1):

Disclosed is a method of reducing crosslinking in gelatin capsules wherein an amino acid and a carboxylic acid are incorporated into the capsule fill, as well as filled gelatin capsules that utilize the disclosed method. The inventive method is especially useful for pharmaceutical formulations which include hydrochlorothiazide, triamterene, gemfibrozil, chloramphenicol, etodolac, piroxicam, nifedipine, tetracycline, diphenhydramine, hydroflumethiazide and rifampin, or a combination thereof as active ingredient.

Brief Summary Text (3):

This invention relates to a method of reducing crosslinking in the gelatin shell of a filled gelatin capsule by incorporating an amino acid and a carboxylic acid into the capsule filling. The inventive filled gelatin capsules possess improved stability relative to filled capsules which do not contain both the amino acid and the carboxylic acid in the filling.

Brief Summary Text (8):

The present invention relates to the discovery that the effects of crosslinking in a gelatin capsule which contains a material that promotes crosslinking are reduced or eliminated by incorporating an effective crosslinking-reducing amount of a combination of at least one amino acid and at least one carboxylic acid in the capsule fill. Both the amino acid and the carboxylic acid are required to obtain the beneficial effects of the present invention.

Brief Summary Text (10):

The present invention relates to a method of reducing crosslinking in a filled gelatin capsule, which filled gelatin capsule consists essentially of a gelatin shell and a filling which is encapsulated by the gelatin shell, wherein the filling comprises a material which promotes crosslinking in the gelatin shell, which method comprises incorporating into the filling an effective crosslinking-reducing amount of a combination of at least one amino acid, or salt thereof, and at least one monomeric carboxylic acid, or salt thereof, which is different from the amino acid and which is in addition to any stearic acid or salt thereof present in the filling; especially wherein the material which promotes crosslinking in the gelatin shell is a pharmaceutical active ingredient or a pharmaceutically acceptable excipient, or a combination thereof.

Brief Summary Text (14):

It is a routine matter to determine whether a material in the capsule filling is causing crosslinking in the capsule shell. For example, the capsule filling contains a material that promotes crosslinking if pellicle formation, and therefore slowed dissolution, is observed during accelerated stability studies, such as storage at 85 percent relative humidity and 40.degree. C. for four weeks. In general, the term "slowed dissolution" is intended to mean that the average dissolution at 45 minutes is reduced by at least 20 percent after the capsules are subjected to the above accelerated stability study conditions. Alternatively, the presence of formaldehyde in the capsule after it is stored under the accelerated

stability study conditions set forth above is also a clear indication that the filling contains a material which promotes crosslinking in the gelatin capsule shell.

Brief Summary Text (38):

Pellicle formation due to crosslinking is also promoted by placing a gelatin capsule in contact with certain packaging materials, for example rayon. According to the present invention, it is also possible to reduce or prevent crosslinking in the capsule shell that is promoted by a packaging material which is in contact with the gelatin capsule. Thus, the present invention further relates to a method of reducing crosslinking in a gelatin capsule, which gelatin capsule is in contact with a material that promotes crosslinking in the gelatin capsule, which method comprises incorporating into the gelatin capsule an effective crosslinking-reducing amount of a combination of at least one amino acid, or salt thereof, and at least one monomeric carboxylic acid, or salt thereof, which is different from the amino acid and which is in addition to any stearic acid or salt thereof present in the filling.

CLAIMS:

1. A method of preparing a filled gelatin capsule wherein the dissolution profile at 45 minutes of capsules maintained at about 40.degree. C. and 85 percent relative humidity for four weeks remains within ± 10 percent of the initial dissolution of the capsules at 45 minutes and/or the dissolution profile at 45 minutes of capsules maintained at about 40.degree. C. and 85 percent relative humidity for twelve weeks remains within ± 20 percent of the initial dissolution of the capsules at 45 minutes, which comprises incorporating into the filled gelatin capsule a material which promotes crosslinking in the gelatin capsule and from 0.1 to 25 percent by weight of at least one monomeric amino acid, or salt thereof, and from 0.01 to about 10 percent by weight of at least one monomeric carboxylic acid, or salt thereof, which is different from the amino acid and which is in addition to any stearic acid or salt thereof present in the filling.

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L14: Entry 17 of 45

File: PGPB

May 23, 2002

DOCUMENT-IDENTIFIER: US 20020061332 A1

TITLE: Amino acid modulated extended release dosage form

Summary of Invention Paragraph:

[0013] Amino acids such as glycine find frequent use as plasticizers in polymer film coatings, as buffering agents and excipients used in the stabilization and formulation of lyophilized products, injectables, nose drops and oral solutions. For example, DL-leucine has been used as a hydrophilic lubricant. Ibsen, U.S. Pat. No. 5,288,500, discloses the possible use of amino acids in combination with hydrophilic polymers to enhance rapid swelling in order to mask grittiness and taste in formulations of granules that are to be rapidly dispersed in water prior to ingestion. Adesunloye, U.S. Pat. No. 5,874,106, discloses that amino acids in combination with carboxylic acids such as citric acid, prevent cross-linking in gelatin capsules. Finally, Thombre et al., U.S. Pat. No. 5,697,922, describe an osmotic device wherein solubility adjusting substances, which may simultaneously act as osmoagents, can be made into coated macro particles. These solubility adjusting substances may include ionizing substances, salts, surfactants or amino acids.

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L2: Entry 23 of 37

File: USPT

Feb 4, 2003

DOCUMENT-IDENTIFIER: US 6514524 B1

**** See image for Certificate of Correction ****

TITLE: Orally administerable immediate-release and prolonged-release galenic form comprising an absorption-promoting agent and use of this absorption-promoting agent

Brief Summary Text (93):

The galenic forms of the invention may be provided in the form of microgranules which may be packaged in a unit dose such as a gelatin capsule, a cachet or a sachet, or even a vial. In this case, the microgranules are obtained by combining the active ingredient and the absorption-promoting agent with one or more excipients chosen from the following categories: Diluents such as calcium carbonate, calcium sulphate dihydrate, sucrose, lactose, dextrates, dextrin, dextrose, dicalcium phosphate dihydrate, kaolin, magnesium carbonate, magnesium oxide, maltodextrin, microcrystalline cellulose, sorbitol, mannitol, starches, talc, tricalcium phosphate. Thickening agents of the lipid type, among which are vegetable oils (cotton seed, sesame and groundnut oils) and derivatives of these oils (hydrogenated oils such as hydrogenated castor oil, glycerol behenate). Thickening agents of the waxy type such as natural carnauba wax or natural beeswax, synthetic waxes such as cetyl ester waxes. Thickening agents of the amphiphilic type such as polymers of ethylene oxide (polyoxyethylene glycol of high molecular weight between 4000 and 100000) or propylene and ethylene oxide copolymers (poloxamers). Thickeners of the cellulosic type (semisynthetic derivatives of cellulose, hydroxypropylmethylcellulose, hydroxypropylcellulose, hydroxymethylcellulose, of high molecular weight and high viscosity, gum) or any other polysaccharide such as alginic acid. Thickening agents of the polymeric type such as acrylic acid polymers (such as carbomers). Thickening agents of the mineral type such as colloidal silica, bentonite. Antioxidants such as ascorbic acid, ascorbyl palmitate, fumaric acid, sodium ascorbate, sodium metabisulphite. Effervescent mixtures are some of the agents capable of being incorporated into the microgranules. These mixtures are composed, on the one hand, of alkali or alkaline-earth metal carbonates or sodium glycin carbonate, and, on the other hand, of organic acids such as citric acid or tartaric acid. Polymers of the cellulosic type (hydroxypropylmethylcellulose, hydroxypropylcellulose, hydroxymethylcellulose, of high molecular weight and high viscosity) or any other polysaccharide such as alginic acid or of polyacrylic type (carbomers) may also be used in combination. This combination makes it possible to obtain microgranules having good floatability in biological media.

Current US Original Classification (1):424/450Current US Cross Reference Classification (1):424/400Current US Cross Reference Classification (2):424/456Current US Cross Reference Classification (3):424/460

Current US Cross Reference Classification (4):
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File: USPT

Jan 29, 2002

DOCUMENT-IDENTIFIER: US 6342249 B1

TITLE: Controlled release liquid active agent formulation dosage forms

Detailed Description Text (36):

The dosage form may contain an antioxidant to slow or effectively stop the rate of any autoxidizable material present in the dosage form, particularly if it is in the form of a gelatin capsule. Representative antioxidants comprise a member selected from the group of ascorbic acid; alpha tocopherol; ascorbyl palmitate; ascorbates; isoascorbates; butylated hydroxyanisole; butylated hydroxytoluene; nordihydroguaiaretic acid; esters of garlic acid comprising at least 3 carbon atoms comprising a member selected from the group consisting of propyl gallate, octyl gallate, decyl gallate, decyl gallate; 6-ethoxy-2,2,4-trimethyl-1,2-dihydroguinoline; N-acetyl-2,6-di-t-butyl-p-aminophenol; butyl tyrosine; 3-tertiarybutyl-4-hydroxyanisole; 2-tertiary-butyl-4-hydroxyanisole; 4-chloro-2,6-ditertiary butyl phenol; 2,6-ditertiary butyl p-methoxy phenol; 2,6-ditertiary butyl-p-cresol; polymeric antioxidants; trihydroxybutyro-phenone physiologically acceptable salts of ascorbic acid, erythorbic acid, and ascorbyl acetate; calcium ascorbate; sodium ascorbate; sodium bisulfite; and the like. The amount of antioxidant used for the present purposes is about 0.001% to 25% of the total weight of the composition present in the dosage form. Antioxidants are known to the prior art in U.S. Pat. Nos. 2,707,154; 3,573,936; 3,637,772; 4,038,434; 4,186,465 and 4,559,237.

Current US Original Classification (1):

424/473

Current US Cross Reference Classification (1):

424/468

Current US Cross Reference Classification (2):

424/472

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| <u>L2</u> | L1 and 424/\$.ccls. | 37 | <u>L2</u> |
| <u>L1</u> | (\$ulfite or \$sulphite) same (gelatin adj3 capsule) | 203 | <u>L1</u> |

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L2: Entry 4 of 4

File: USPT

Mar 7, 2000

DOCUMENT-IDENTIFIER: US 6034138 A

TITLE: Disinfectant composition

Detailed Description Text (4):

The invention comprises a solid or semi-solid composition that forms a sterilizing solution upon the addition of water. The solid or semi-solid composition comprises a protected sterilant, an alkaline salt to facilitate regeneration of the aldehyde, and a liberating oxidizing agent that reacts with the protective moiety when generated in solution to prevent regression of the aldehyde back to its derivative state. For purposes of the present application, a "solid or semi-solid" composition includes such forms as powders, traditional tablets, coated tablets, injection molded solids, soft or hard gelatin capsules, gels, ointments, creams and the like.

Detailed Description Text (7):

Preferred protecting agents are those that readily form covalent bonds with the selected sterilant. Such compounds are known as addition compounds. With glutaraldehyde, groups providing sulfite and oxime ligands to the aldehyde moieties are preferred, and sulfite ligands are especially preferred. Salts of these ligands, especially soluble alkali salts are most preferred due to the relative ease of solubilization.

Detailed Description Text (11):

The problem that arises then is that at the higher pH environments wherein glutaraldehyde formation from the bisulfite addition compound is favored, the polymerization and deactivation of glutaraldehyde is also favored. It was discovered that one way in which glutaraldehyde can be completely liberated from the bisulfite protective group once it is dissolved in solution at lower pH values is by shifting the equilibrium of the reaction toward glutaraldehyde formation while using a suitable buffer to hold the pH range from 8.0 to 8.5, the optimal operating range of most commercial glutaraldehyde based sterilants. This is accomplished by removing sulfite from the right side of the reaction equation by oxidizing it to sulfate. With the sulfite converted to sulfate, the reverse reaction of glutaraldehyde with sulfite is eliminated. The problem, of course, especially with glutaraldehyde, is to selectively oxidize the sulfite without also oxidizing the aldehyde groups of glutaraldehyde. Aldehyde groups are easily oxidized to carboxylate groups, which have no antimicrobial activity.

Detailed Description Text (12):

The equilibrium driving agent may be any compound that reacts with the dissociated sulfite or oxime protective ligand in preference to the aldehyde groups of the sterilant. It was discovered that preferred agents for oxidizing the protecting ligand include the alkali and alkaline earth metal salts of: percarbonates; persulfates; hypochlorites; superoxides; chlorites; peroxyacetates; hypobromites; hypiodites; perborates; periodates; peroxides; peroxyformates; peroxybenzoates; chlorates; bromites; and chloroperoxybenzoates. More preferably, especially for GBS compounds, the oxidizing agents are sodium perborate and sodium percarbonate.

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L5: Entry 17 of 18

File: USOC

May 21, 1957

DOCUMENT-IDENTIFIER: US 2793160 A

TITLE: Poliomyelitis vaccine

OCR Scanned Text (1):

H3 killed poliomyelitis vaccine composed of killed but antigenic poliomyelitis viruses of types 1, 2 and 3 has been developed and has undergone exhaustive emeal testing. This poliomyelitis vaccine is, like many other vaccines, an aqueous preparation which is administered by injection. Because of this it is essential that the vaccine be sterile, that is, free from contaminating bacteria, molds and fungi not only at the time of manufacture and packaging but also at the time of administration. . . . It is, perhaps at least theoretically, possible to prepare and package the vaccine under aseptic conditions, such vaccines at the time of administration may well be contaminated, particularly as a multiple dose package. Moreover, manufacturing under completely aseptic conditions is prohibitive from a cost standpoint and completely impractical. In an attempt to insure that the poliomyelitis vaccine will be free from contaminating bacteria, molds and fungi, and to safely remain so it has been proposed to add a mercurial, specifically thimerosal, as a preservative. While this expedient has provided a solution to the problem of contamination it has given rise to another and perhaps even more serious problem, namely, that the 50 thimerosal causes the poliomyelitis vaccine to lose its potency. Because of this poliomyelitis vaccine products containing thimerosal as a preservative must be administered soon after their manufacture. This is, of course, highly undesirable because the vaccine is difficult and expensive to prepare and under such circumstances production must be limited to anticipated short term requirements. In view of this and because the vaccine requires several months to prepare, it is impractical to produce sufficient vaccine to meet unexpected emergency demands. 60 There is therefore a pressing need for a poliomyelitis vaccine product which will not only be safely free from contaminating bacteria, fungi and molds at the time of administration but which will also retain its potency, that is, its antigenicity, over a considerable period of time under normal conditions of storage. It is an object of the present invention to provide a poliomyelitis vaccine product which remains safely free from contaminating bacteria, molds and fungi over a considerable period of time under normal conditions of storage and use by physicians. 2 1 7 9 3 @ 1 6 0 United States Patent Office i, . it is also object of the invention to provide a poliomyelitis vaccine product which retains its antigenicity over 2,793,160 -@i, considerable -@eriod -of time -under normal conditions of storage. POLIOMYELITIS VACCINE 5 Surprisingly both of these objects as well as other objects of William McLean, Jr., Gr6s@b Pointo, Mich.; -assignor to which will appear hereinafter can be realized and the Parke, Davis & Company, Detroit Mich, a corporation - aforementioned - difficulties with poliomyelitis vaccine production of Michigan products overcome in accordance with the invention, by incorporating into, a "killed" poliomyelitis vaccine, i. e., an inactivated poliomyelitis vaccine. Application-May 9, 1955, Serial No. 507 163 20 aqueous solution containing non-infectious but antigenic poliomyelitis virus, a substance belonging to a class of 7 Clohns. (Cl. 167-78) compounds known to be protein precipitants and denaturants. More particularly, the present invention comprises incorporating benzethonium chloride in an aqueous solution of poliomyelitis vaccine products and to 15 killed poliomyelitis vaccine in a concentration, grams per milliliter (>ds for preparing the same., More particularly, the millifilter; in the range from about

1:20,000 to 1@50,000. invention relates to poliomyelitis -vaccin@-products and to The benzethonium chloride is preferably incorporated in methods for preparing t@e, sme. -the vaccine by'slowly addiing a dilute aqueous solution As is known, poliomyelitis is a vrius disease which may of -the benzethonium chlorider to the aqueous killed polio- be fatall or have far-reaching crippling effects. Because 20 myelitis vaccine, with -effidebt stirring. Chemically benz- of the nature of the disease, the only sound approach to ethonium chloride is, known: as benzyldimethyl [2-(2-ethoxy) - ethyl]am- to prevent the occurrence of the disease. Recently, a monium chloride monohydrate andhas the fonnula ClEl's CII, CE3 I 1+ -H2o CHR- -CHR- C O 7 C H 2 7 - Q H I - - O - C H 2 - - C H I - N - C E 3 c c i c 'The preferred products are those which contain benz'.ethonium chloride in a concentration in the range from 30 -'i--2'0,000 to 1:40,000. -@The @a4ue6us killed poliomyeliti s vaccines used in the @r6duction of prod,4cts of the invention can ccintaffi any or aU of the vari Ous .. tYPes of poliomyelitis virus. The @r6ferred vaccines are 'thosef wh- ich cofitain types 1, 2 and '!'Of P6ji H' ' ' - 35 omy e tisvi rus. Part i.cul arly suit able vac cine sare ihose which are relati@ely low in protein content, preferably those :which . con-tain less than aboiit 1.8 to 70 ro m nitrogen. Suich vacciies can ,ganim,a per ml. of p te' b@ produe'd i -n a number of different ways. For example, ticularly if the packagd is what is, commonly known in 40 macerated 'monk@y kidney tiss can be trypsinized to . u e in, iemp e extraneous t ue, the residual cells allowed tb niuliiply, the mediuni inoculated with the poliomyelitis virus, the- mixture.incu] 5ated, the fluid harvested and the living virus inactivated b'y treatrnt with formaldehy4 e 7@ltraviolet radiation or other suitable means. If desired vaccines prepared by omission of the trypsinization step' can also be used but in this instance the protein content of - the vaccine may be excessively high and should be assayed before use. iii the preparation of mixed vaccines, that is, vac - cines containing more than one type of poliomyelitis virus, it is customary to pc>ol or mix the harvested fluids containing the various types subsequent to -the inlactivation step although, if desired, this can be done preliminarily. When using formaldehyd e inactivated vaccines, best results in accordance with the invention are obtained by the use of vaccines to which no sodium bisulfite has been added to reduce the form- aldehyde content. The invention, is fllustrated by the following - examples. EXAMPLE I Cells for the cultivation of poliomyelitis virus are prepared by the method of Dulbecco, Journal of Experiment @l Medicine, 99,)@age 167 (1954). Briefly, this procedure consists in first prepatng a suspensign of mcnkey kidney epithelial cells [see - Dulbecco, Proc. Nat. Acad. Sci., 38, page 747 (1952)] by treating macerated kidnqy tissu-e from healthy Cynomal-gus or Rhesus monkeys with trypsin to remove extraneous matter -and release the individual cells. Tbe-se cells are allowed to multiply on a suitable giass sur-face in any of a number of tissue culture mediums. The sheet of cultivated kidney cells thus pro-

Current US Original Classification (1):

424/217.1

Current US Cross Reference Classification (1):

424/278.1

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